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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/056,420	01/24/2002	Ronald B. Moss	P-IM 5158	8063

41552 7590 04/27/2006

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EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 04/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/056,420	MOSS ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 03 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Office Action

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the communication received 29 December, 2005. No claim amendments accompanied the response. Claims 1-26 are pending in the instant application.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and usé the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 1-26 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims. The claims are broadly directed toward a method of treating HIV-infected individuals through structured treatment interruptions (STIs) with immune-based therapies. Antiviral therapy is ceased and patients are immunized with an "HIV immunogenic composition" that presumably leads to an immune system boost.

As previously set forth, the legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth. *Enzo Biochem, Inc.*, 52 U.S.P.Q.2d 1129

(C.A.F.C. 1999). *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

1) The state-of-the-art as it pertains to HIV-1 and -2 vaccine development is replete with failure. To date, there are no successful HIV-1 or -2 vaccines. The failure to identify and develop suitable immunogenic compositions has been due to several factors including: (i) the failure to identify the correlates of protective immunity; (ii) the failure to identify suitable immunogens, adjuvants, routes of administration, and immunization regimens; (iii) the quasispecies nature of lentiviral infection which leads to immune escape, and (iv) the lack of an adequate animal model that is reasonably predictive of clinical efficacy (Haynes *et al.*, 1996; Lee, 1997; Letvin, 1998; Burton and Moore, 1998; Johnston, 2000; Feinberg and Moore, 2002).

Based upon the proffered exhibits, Applicants appear to have identified a **single immunogen** (e.g., **REMUNE**) that appears to provide a positive clinical effect under carefully specified conditions (i.e., selection of patient population, immunization protocol, STI regimen, etc.). Applicants are reminded that none of these limitations appear in the broadest claim. Moreover, the identification of a single immunogen in the face of continuing vaccine failure is insufficient to enable the full breadth of the

claimed invention.

2) The disclosure fails to provide adequate guidance pertaining to the correlates of protective or therapeutic immunity. In order to assess the true effectiveness of any given immunogen, the skilled artisan would need to know the nature, duration, and specificity of the immune response that confers a salubrious effect on the patient. However, the disclosure fails to provide any guidance pertaining to this subject. Applicants' exhibits and arguments appear to suggest that T_h responses in conjunction with HIV-1-specific CTL responses, under limited circumstances, may provide a clinical benefit. Applicants are again reminded that none of these parameters appear in the broadest claim language.

3) The disclosure fails to provide adequate guidance pertaining to the preparation of suitable immunogens, adjuvants, routes of administration, and immunization regimens. In order to practice the claimed invention, the skilled artisan would require a knowledge of these parameters. However, the disclosure is silent pertaining to these various parameters. As noted *supra*, the immunogen REMUNE is the only disclosed immunogen. Considering the previous failures of other HIV immunogens, a single embodiment is insufficient to enable the full breadth of the claimed invention directed toward any sundry immunogenic composition.

4) The disclosure fails to provide any working embodiments. It was noted that the disclosure provided some preliminary data from a small clinical sample involving the immunogen REMUNE. However, this data cannot be relied upon at this point in time for enablement purposes. It is not readily apparent from reviewing the data that the STI regimen followed by REMUNE immunization was actually providing a therapeutic or protective immune response. The example failed to provide details about the immunological status of each patient participating in the trial. The study failed to measure meaningful immunological and virological indices

that would be predictive of vaccine efficacy.

5) The claims are of considerable breadth and encompass any "HIV immunogenic composition." As noted *supra*, there are a number of limitations associated with vaccine development including the identification of suitable immunogens and the correlates of protective immunity. The disclosure fails to provide adequate support for an given HIV immunogen. Applicants' response does not overcome this aspect of the rejection.

Accordingly, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention.

Additional Arguments

Applicants again rely upon previously submitted exhibits to demonstrate that the invention is fully enabled. These exhibits were addressed individually in the last office action. As previously set forth:

-Exhibit A: "Guidelines for use of antiretroviral agents" has been considered but the particular relevance of this exhibit is not readily manifest. The examiner is not questioning the guidelines associated with antiretroviral treatment but rather is questioning which immune and virological response in any given study are reasonably predictive of clinical success. For instance, does the patient population require a minimum $CD4^+$ cell count and maximum viral load? After administering any given immunogen, which parameters are reasonably predictive of a positive clinical outcome?

Exhibit B: The teachings of Moss *et al.* (2003) have been considered. However, this publication is insufficient to enable the full breadth of the claimed invention. First, this study administered a single HIV immunogen, REMUNE. No other suitable HIV immunogens were described. Second, this study demonstrated that

REMUNE was only effective after the SECOND STI. Third, there was no indication in this study that the correlates of protection/therapy were generated.

Exhibit C: The teachings of Lichterfeld *et al.* (2004) are also insufficient to overcome the rejection. First, this study also administered a single HIV immunogen, REMUNE. No other suitable HIV immunogens were described. Second, a specific immunization regimen was employed that required at least four doses of the composition. Finally, although generic $CD4^+$ and $CD8^+$ proliferative responses were observed, there was no demonstration that these response were of a high-titer neutralizing nature.

Exhibit D: Fernandez-Cruz *et al.* (2004) reported that under specific conditions statistically significant differences were noted with REMUNE when both the viral load and $CD4^+$ cell count were taken into consideration. Thus, it appears that with patients displaying high viral loads and low $CD4^+$ counts after STI, the immunization/STI regimen will not work. In fact the authors cited another study involving REMUNE (Kahn *et al.*, 2000) wherein positive immune responses were NOT obtained.

Exhibits E and F: Both of these studies employed a specific immunogen (e.g., REMUNE) and specific study conditions which do not appear in the claim language. Accordingly they are insufficient to enable the full breadth of the claim language.

Finality of Office Action

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). **A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE**

SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, James C. Housel, can be reached at (571) 272-0902. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access

to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

18 March, 2006